EFFECT OF CONTRAST ON SYSTOLIC MYOCARDIAL ULTRASOUND COLOR-DOPPLER VELOCITY

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Abstract-**Intravenously distributed ultrasound contrast increases echoes from the normally low echogenic bloodpool and myocardial perfusion imaging is developing. However the microspheres used are potential endothelial stimulators as well as nonlinear scatterers. Tissue Doppler is developed to detect velocities of myocardial motion, which are in the same range as perfusion flow velocities. The effect of contrast is not evaluated. We performed echocardiography in 12 patients with ischemic heart disease before and immediately after a slow intravenous infusion of 27 ml Optison â using color myocardial Doppler imaging (GE Vingmed systemV). Longitudinal basal systolic velocities and their integrals were analyzed in digitally stored cineloops. Peak mean velocity increased 10% by contrast from mean 5.2± 1.8 (SD) to 5.7± 2.3 cm/s (p=0.02, confidence interval 2-16%) but integral did not change (0.8±0.4 cm). Contrast has no effect on blood pressure or heart rate in used dose. It is therefore of interest to further evaluate if this increase in velocity; a) is a methodological effect that may be used to detect contrast within myocardium (and thereby perfusion / blood volume), or b) is secondary to increased flow and motion caused by endothelial and vascular effects from the contrast microspheres. Either have important methodological, physiological and clinical impact.**

Keywords **Ultrasound Tissue Doppler, Myocardial Contrast, Perfusion, Physiology, Methodology**

I. INTRODUCTION

Myocardial contrast echocardiography is a rapidly increasing area after the introduction of new imaging modalities and contrast agents [1, 2] . Microspheres stable enough to pass the pulmonary circulation enables left heart enhancement after intravenous administration. Gas encapsulated in shells with different acoustic behavior makes the returned signal specifically reshaped. The detection of single bubbles within the micro-circulation is therefore possible and has numerous applications within the ischemic heart disease area as well as for pharmaceutical and pato-physiological evaluation of myocardial perfusion effects. Left side ultrasound contrast agents are today registered for blood pool enhancement [3] .

Visualization of myocardial flow and blood volume have until lately been dependent on relatively high power output used in order to destroy the microbubbles [4] . There are no reported hemodynamic effects from registered contrast agents when used as in clinical practice. Experimental designs however, show that the combination of high output echocardiography and contrast agents have effects on levels and uptake of vascular endothelial growth factors (VEGF)[5] . VEGF is know to stimulate angiogenesis and dilatation, the latter probably due to both shear-stress-related and direct effects [6, review] .

When exposed to ultrasound, the microbubbles oscillate, and also generate harmonics at medium transmitted power. At high power output they rupture [7] and the returning pulse changes radically. How contrast agents with the above mentioned acoustical responses, affects measurements with color tissue Doppler imaging [8] , developed for myocardial motion analysis, is to our knowledge not evaluated. Myocardial motion is slower than intracardiac blood flow and the relatively low velocities are comparable to those seen in the microcirculatory flow. An appealing possibility would be if contrast (i.e. blood) motion could be distinguished from tissue motion using Tissue Doppler, either in pulsed mode, or in color mode. The aim of this study was to evaluate the effect of contrast on color tissue Doppler images and their velocity estimates in a clinical setting.

II. METHODOLOGY

1) *Patients*. Twelve patients with known ischemic heart disease and from scintigrams diagnosed perfusion defects participated. They were between 50 and 80 years old (mean±SD 63±10) and 5 were female.

2) *Echocardiography*. In left supine position apical two and four chamber views were obtained. Two heartbeat cineloops with superimposed color tissue Doppler information (2.5MHz, GE Vingmed systemV, Horten, Norway) were digitally stored. Mechanical index was high 1.2 as was framerate (approx. 100 fps) and images were continuously captured with a Nyquist level of 0.25cm/s. Gain was corrected in order not to cause too much blooming effects, otherwise settings were kept unchanged. Registrations were made before and immediately after slow intravenous infusion of 2.7 ml Optison® (Mallinckrodt, Linköping, Sweden), a solution of 2—4.5 um microspheres made of albumin (shells) and perfluorocarbon gas. No adverse effects were registered.

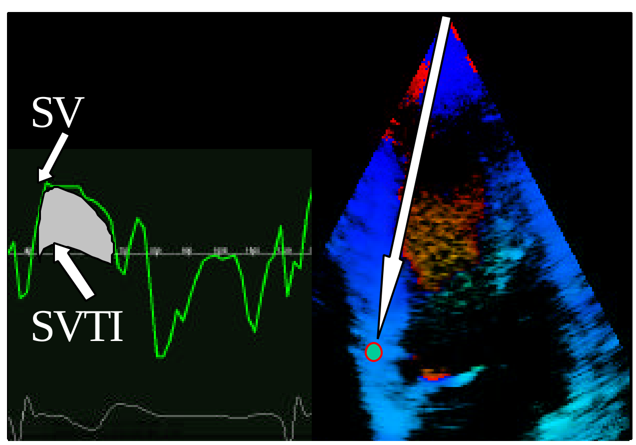

Fig. 1. Illustration of septal analysis (4 chamber view).
SV: Spatial mean peak systolic velocity (cm/s), SVTI: systolic integral.

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3) *Analysis*. Spatial mean peak systolic longitudinal velocity (SV) and its systolic positive integral (SVTI, systolic shortening) were measured in the basal segment of the septal, lateral, posterior and anterior walls, using a comercially available analysis package (Fig.1. EchoPac, GE-Vingmed Sound, Horten, Norway). Values from two heart beats were averaged and results from pre- and post-contrast were compared using the paired two-tailed Student's t-test. A p-value <0.05 was considered significant. The reproducibility of the measurements has been evaluated previously in a multicenter study and coefficients of variation for SV and SVTI are 9-14% and 9-17% respectively [9] .

III. RESULTS

The recorded SV and SVTI in patients were overall low (5.2 ± 1.8 cm/s and 0.8 ± 0.4 cm) when compared to normal values [10] , due to left ventricular dysfunction in ischemic heart disease. After contrast the SV increased approximately 10% to 5.7±2.3 cm/s (p=0.02, 95% confidence interval 2-16%), but integral did not change (p= 0.54). The correlation between the measurements before and after contrast was 0.83 both for SV (Fig. 2) and SVTI.

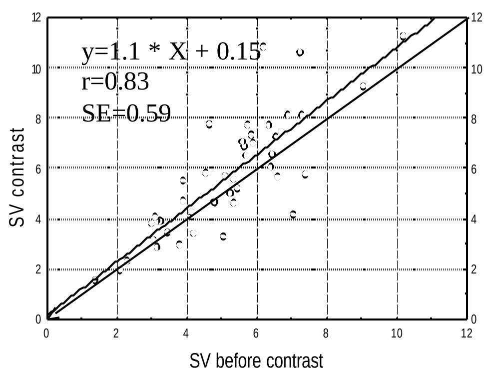

Fig. 2. Linear regression of spatial mean peak myocardial velocities (SV) before and after IV contrast. Line of identity is dotted.

The 95% predictive interval [11] included the zero but a bias of 0.5 cm/s was introduced in systolic velocity but not for integral as a mean value of differences (Figure 3). No bias was introduced when measuring SVTI before and after contrast (mean difference <0.02).

IV. DISCUSSION

Our results show that different velocity based measurements during heart cycle react differently on contrast. We show a 10% increase in spatial mean peak velocity while no consistent change was noted in the systolic integral. However there was a relatively wide range of changes, possibly due to unevenly distributed old myocardial infarctions and

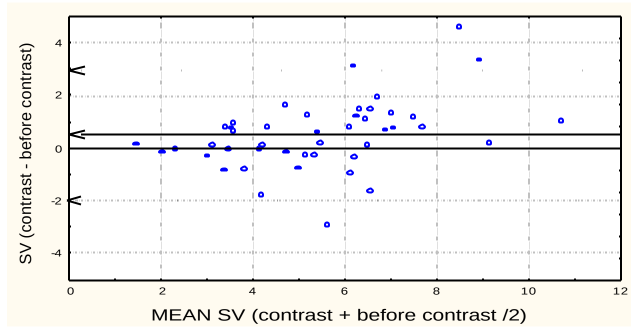

Fig. 2. Mean difference (bias) and 95% predictive intervals (+2SD) when SV before and after contrast are compared (marked by arrows and plotted against mean SV on x-axis).

reproducibility factors. No patient had symptoms or heart rate change during the infusion. However, there are both methodological and physiological aspects that have to be considered.

The unevenly distributed effects indicate that a physiological effect cannot be ruled out. Intracoronary injections of microspheres after PTCA dilate the coronary arteries. One possible explanation is shear stress induced vasodilatation caused by increased levels of NO / prostaglandin resulting in decreased afterload and/or increased coronary flow or motion. Also, VEGF is upgraded by ischemia. Increased uptake of VEGF could be another explanation of vasodilatation. VEGF is known to induce those vasoactive substances, independently of shear stress [12] . This could be possible as the combination of high output echocardiography and contrast agents have effects on VEGF in animals as already mentioned [5] .

Pure methodological effects do not fully explain the differences between SV and VTI. The power output used was high and there is a clear risk that most contrast bubbles already ruptured within the myocardium, in which case there were few bubbles to detect. Bubbles that do rupture, cause random phase shifts [13], which should not consistently increase the velocity estimate. However, bubbles in regions where the acoustic pressure is lower, contribute with harmonic energy, which could alter the estimated velocity [13].

A pure echo-enhancing effect would equal a gain increment, but here the gain was adjusted in the normal way for optimal imaging. The difference is that the microbubbles move slowly relative the myocardial tissue. Bu this motion is presumably isotropic, meaning that the detected velocity should not change.

If further investigation do explain the increased velocity to be a methodological effect, this may be a new way to detect contrast agents that need to be further evaluated.

V. CONCLUSION

Ultrasound contrast agents influence upon velocity estimates of myocardial motion as measured by color tissue Doppler imaging. The reason for the changes might have both physiological and methodological background. Further evaluation will show if the changes are effects secondary to changes in endothelium and vessels or if it is an effect of contrast itself on the ultrasound tissue Doppler signal. Either have important methodological, physiological and clinical impact

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